

**REMARKS**

Claims 45-54 are pending. Applicants add one new claim, claim 55. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter. Support for these amendments appears throughout the specification and claims as filed. No new matter is introduced by these amendments.

**Rejection under 35 U.S.C. § 103(a)**

Claims 45-54 are rejected as unpatentable over Herron (US Patent 4,764,521) in view of Rubenstein (IDS, CJ) and Rephaeli et al. (US Patent 5,939,455); and also over Faller et al. (WO 99/40883). Applicants traverse.

Applicants acknowledge the statements in the Action that Herron and Faller (WO 99/40883) do not expressly teach 4-phenyl-trans-3-butenoic acid for the treatment of cystic fibrosis.

Applicants have amended the claims to recite methods of treating cystic fibrosis involving administration of 4-phenyl-trans-3-butenoic acid (aka trans-styryl acetic acid) and salts thereof. Applicants submit that 4-phenyl-trans-3-butenoic acid exhibits unexpected activity relative to cited art compounds cinnamic acid and 4-PBA. In support of Applicants' assertion, Applicants submit herewith the declaration of Pamela L. Zeitlin, M.D., delineating the experimental protocol and results conducted in her laboratory demonstrating the superior activity of 4-phenyl-trans-3-butenoic acid in promoting the trafficking of functional  $\Delta F508$ -CFTR in model cells of cystic fibrosis (attached w/ exhibits). As such, Applicants submit that the *prima facie* rejection is overcome and respectfully request withdrawal of the rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. (71699) 49632.

Dated: March 5, 2007

Respectfully submitted,

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